

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
5 April 2001 (05.04.2001)

PCT

(10) International Publication Number
WO 01/23528 A1

- (51) International Patent Classification⁷: C12N 5/00
- (21) International Application Number: PCT/US00/26469
- (22) International Filing Date:
27 September 2000 (27.09.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
09/406,253 27 September 1999 (27.09.1999) US
- (63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:
US Not furnished (CIP)
Filed on Not furnished
- (71) Applicants (for all designated States except US): UNIVERSITY OF FLORIDA RESEARCH FOUNDATION [US/US]; 223 Grinter Hall, Gainesville, FL 32611 (US). IXION BIOTECHNOLOGY, INC. [US/US]; Suite N-111, 13709 Progress Boulevard, Box 13, Alachua, FL 32615 (US).
- (72) Inventors; and
(75) Inventors/Applicants (for US only): PECK, Ammon, B. [US/US]; 346 N.W. 50th Boulevard, Gainesville, FL 32607 (US). CORNELIUS, Janet, G. [CA/US]; 6024 N.W. 52nd Terrace, Gainesville, FL 32653 (US). RAMIYA, Vijayakumar, K. [IN/US]; 10323 S.W. 82nd Lane, Gainesville, FL 32608 (US).
- (74) Agents: SWANSON, Barry, J. et al.; Swanson & Bratschun, L.L.C., 1745 Shea Center Drive, Suite 330, Highlands Ranch, CO 80129 (US).
- (81) Designated States (national): AU, CA, KR, MX, US.
- (84) Designated States (regional): European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).
- Published:
— With international search report.
— Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: REVERSAL OF INSULIN-DEPENDENT DIABETES BY ISLET-PRODUCING STEM CELLS, ISLET PROGENITOR CELLS AND ISLET-LIKE STRUCTURES

(57) Abstract: The subject invention concerns new methods which make it possible, for the first time, to grow functional islet-producing stem cells (IPSCs), islet progenitor cells (IPCs) and IPC-derived islets (IdIs) in *in vitro* cultures. The subject invention also concerns the use of the *in vitro* grown IPSCs, IPCs and/or IdIs for implantation into a mammal for *in vivo* therapy of diabetes. The subject invention further concerns a process of using the implanted cells for growing a pancreas-like structure *in vivo* that has the same functional, morphological and histological characteristics as those observed in normal pancreatic endocrine tissue. The ability to grow these cells *in vitro* and pancreas-like structures *in vivo* opens up important new avenues for research and therapy relating to diabetes.

WO 01/23528 A1

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 09 August 2001 (09.08.01)	
International application No. PCT/US00/26469	Applicant's or agent's file reference UF141.C4/PCT
International filing date (day/month/year) 27 September 2000 (27.09.00)	Priority date (day/month/year) 27 September 1999 (27.09.99)
Applicant PECK, Ammon, B. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 23 April 2001 (23.04.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

BEST AVAILABLE COPY

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer CROCI Christelle
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/26469

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 5/00
US CL : 435/325, 377

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/325, 377

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EAST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,834,308 A (PECK et al) 10 November 1998, see entire document.	1-45
Y	US 5,681,587 A (HALBERSTADT et al) 28 October 1997, see entire document.	1-45

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

30 November 2000 (30.11.2000)

Date of mailing of the international search report

01 FEB 2001

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703)305-3230

Authorized officer

L Blaine Lankford

Telephone No. 308-0196

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

RECD 23 AUG 2001

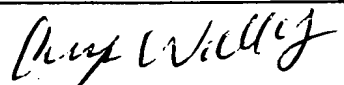
Applicant's or agent's file reference UF141.C4/PCT	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/26469	International filing date (day/month/year) 27 September 2000 (27.09.2000)	Priority date (day/month/year) 27 September 1999 (27.09.1999)	
International Patent Classification (IPC) or national classification and IPC IPC(7): C12N 5/00 and US Cl.: 435/325,377			
Applicant UNIVERSITY OF FLORIDA RESEARCH FOUNDATION			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
 - I ☒ Basis of the report
 - II ☐ Priority
 - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 23 April 2001 (23.04.2001)	Date of completion of this report 18 June 2001 (18.06.2001)
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer: L Blaine Lankford  Telephone No. 308-0196

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/26469

I. Basis of the report**1. With regard to the elements of the international application:***

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-55 _____ as originally filed
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.
- ☒ the claims:
pages 56-61 _____, as originally filed
pages NONE _____, as amended (together with any statement) under Article 19
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.
- ☒ the drawings:
pages 1-19 _____, as originally filed
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE _____, as originally filed
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/26469

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)

Claims 1-45 YES
Claims NONE NO

Inventive Step (IS)

Claims 1-45 YES
Claims NONE NO

Industrial Applicability (IA)

Claims 1-45 YES
Claims NONE NO

2. CITATIONS AND EXPLANATIONS (Rule 70.7)

Claims 1-45 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a method of growing IPSCs, IPCs and Idls wherein the cells produced are effective to treat pancreatic diseases.

----- NEW CITATIONS -----